Variable Heavy

```
A4.6.1      EIQLVQSGPELKQPGETVRISCKASGYTFTNYGMNWVKQAPGKGLKWMG
             *   *  **  *   ***  *  *                *      * *
F(ab)-12    EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWVRQAPGKGLEWVG
                                        *  **  *  *           *
humIII      EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS
            1        10         20         30         40

A4.6.1      WINTYTGEPTYAADFKRRFTFSLETSASTAYLQISNLKNDDTATYFCAK
                                    *  *      *** ***   * *
F(ab)-12    WINTYTGEPTYAADFKRRFTFSLDTSKSTAYLQMNSLRAEDTAVYYCAK
            * **** ***  *** *   * * *  * *                  *
humIII      VISGDGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
          50  a       60         70         80  abc       90

A4.6.1      YPHYYGSSHWYFDVWGAGTTVTVSS (SEQ ID NO:9)
                          *  *
F(ab)-12    YPHYYGSSHWYFDVWGQGTLVTVSS (SEQ ID NO:7)
            *            *
humIII      G----------FDYWGQGTLVTVSS (SEQ ID NO:11)
                         110
```

Fig. 1A

Variable Light

```
A4.6.1      DIQMTQTTSSLSASLGDRVIISCSASQDISNYLNWYQQKPDGTVKVLIY
                  **      *    * *                 ****
F(ab)-12    DIQMTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQKPGKAPKVLIY
                                    *  *     *          *
humKI       DIQMTQSPSSLSASVGDRVTITCRASQSISNYLAWYQQKPGKAPKLLIY
            1        10         20         30         40

A4.6.1      FTSSLHSGVPSRFSGSGSGTDYSLTISNLEPEDIATYYCQQYSTVPWTF
                                 **    * *  *
F(ab)-12    FTSSLHSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYSTVPWTF
            **   *                                      ***
humKI       AASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSLPWTF
          50         60         70         80         90

A4.6.1      GGGTKLEIKR (SEQ ID NO:10)
             *   *
F(ab)-12    GQGTKVEIKR (SEQ ID NO:8)

humKI       GQGTKVEIKR (SEQ ID NO:12)
          100
```

Fig. 1B

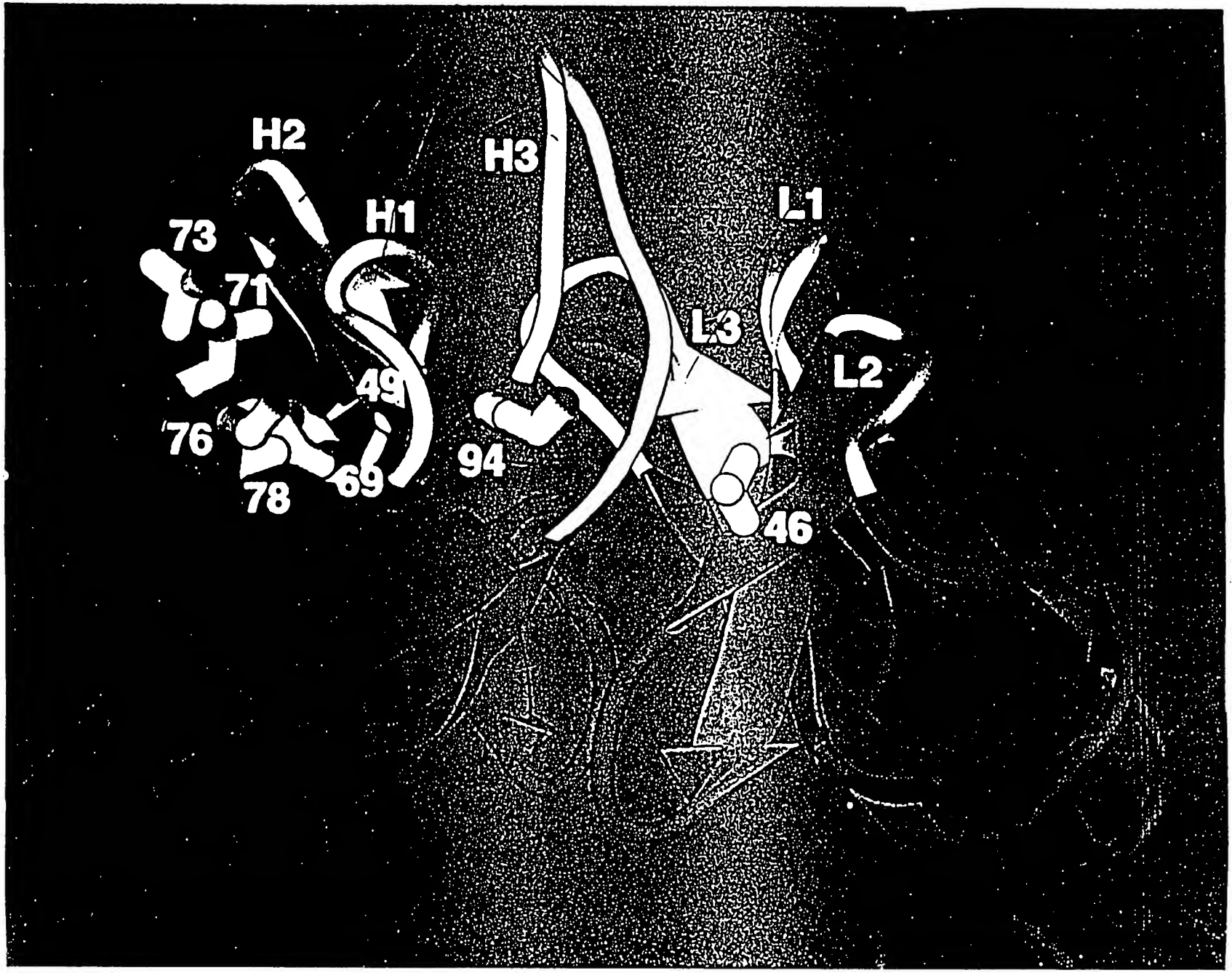

Fig. 2

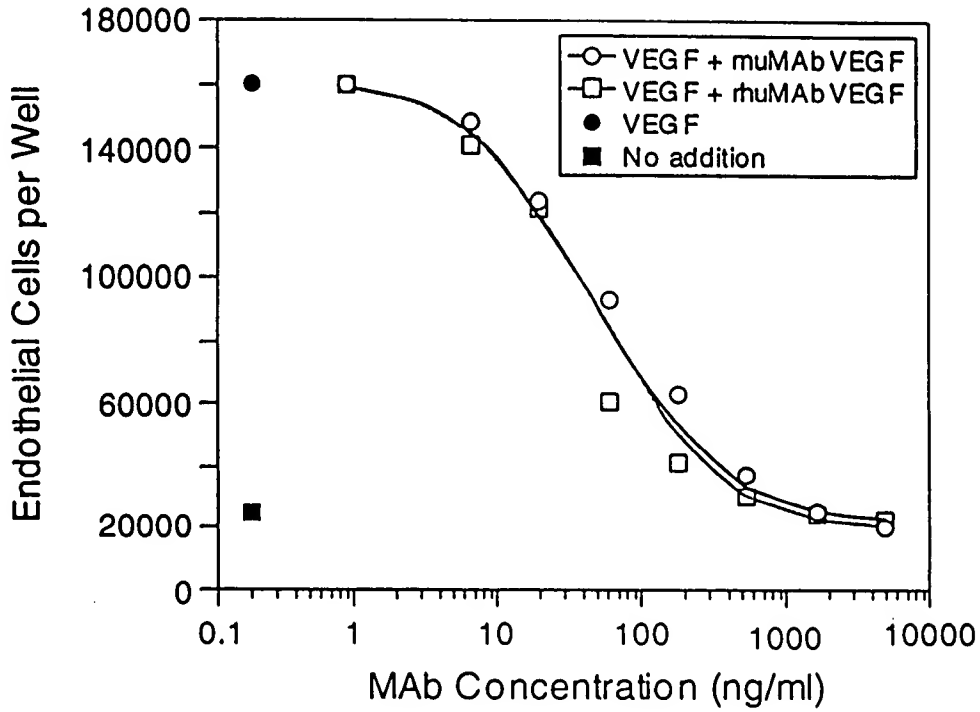
180000
140000
100000
60000
20000
0
Endothelial Cells per Well
0.1
1
10
100
1000
10000
MAb Concentration (ng/ml)
VEGF + muMAb VEGF
VEGF + rhuMAb VEGF
VEGF
No addition

Fig. 3

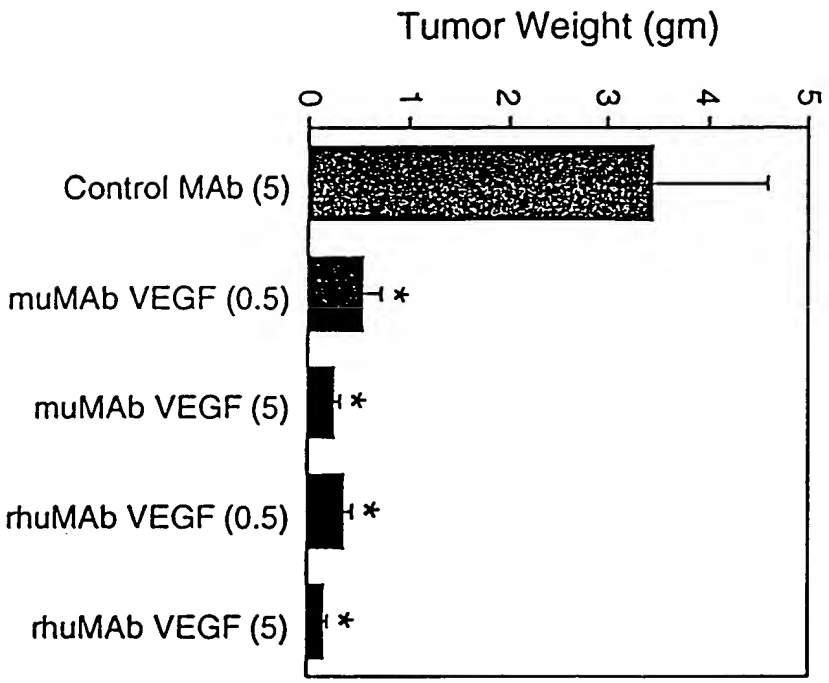
Tumor Weight (gm)
0
1
2
3
4
5
Control MAb (5)
muMAb VEGF (0.5)
muMAb VEGF (5)
rhuMAb VEGF (0.5)
rhuMAb VEGF (5)
*
*
*
*

Fig. 4

V_L domain

```
                10        20        30        40
A4.6.1  DIQMTQTTSSLSASLGDRVIISCSASQDISNYLNWYQQKP
          **      *   * *
hu2.0   DIQMTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQKP

hu2.10  DIQMTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQKP

                50        60        70        80
A4.6.1  DGTVKVLIYFTSSLHSGVPSRFSGSGSGTDYSLTISNLEP
        **** *                          **   * *
hu2.0   GKAPKLLIYFTSSLHSGVPSRFSGSGSGTDFTLTISSLQP
                                        .
hu2.10  GKAPKLLIYFTSSLHSGVPSRFSGSGSGTDYTLTISSLQP

                90       100
A4.6.1  EDIATYYCQQYSTVPWTFGGGTKLEIK (SEQ ID NO:10)
          *                 *   *
hu2.0   EDFATYYCQQYSTVPWTFGQGTKVEIK (SEQ ID NO:13)

hu2.10  EDFATYYCQQYSTVPWTFGQGTKVEIK (SEQ ID NO:15)
```

Fig. 5A

V_H domain

```
                10        20        30        40
A4.6.1  EIQLVQSGPELKQPGETVRISCKASGYTFTNYGMNWVKQA
          *   *  ** *   *** * *                *
hu2.0   EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWVRQA
                                          .
hu2.10  EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWIRQA

                50 a      60        70        80
A4.6.1  PGKGLKWMGWINTYTGEPTYAADFKRRFTFSLETSASTAYL
          * *                   * *** ** *
hu2.0   PGKGLEWVGWINTYTGEPTYAADFKRRFTISRDNSKNTLYL
                                  . . .. .
hu2.10  PGKGLEWVGWINTYTGEPTYAADFKRRFTISLDTSASTVYL

              abc      90       100abcdef       110
A4.6.1  QISNLKNDDTATYFCAKYPHYYGSSHWYFDVWGAGTTVTVSS (SEQ ID NO:9)
        *** ***   * *  *                   *  *
hu2.0   QMNSLRAEDTAVYYCARYPHYYGSSHWYFDVWGQGTLVTVSS (SEQ ID NO:14)
                          .
hu2.10  QMNSLRAEDTAVYYCAKYPHYYGSSHWYFDVWGQGTLVTVSS (SEQ ID NO:16)
```

Fig. 5B

Fig. 6

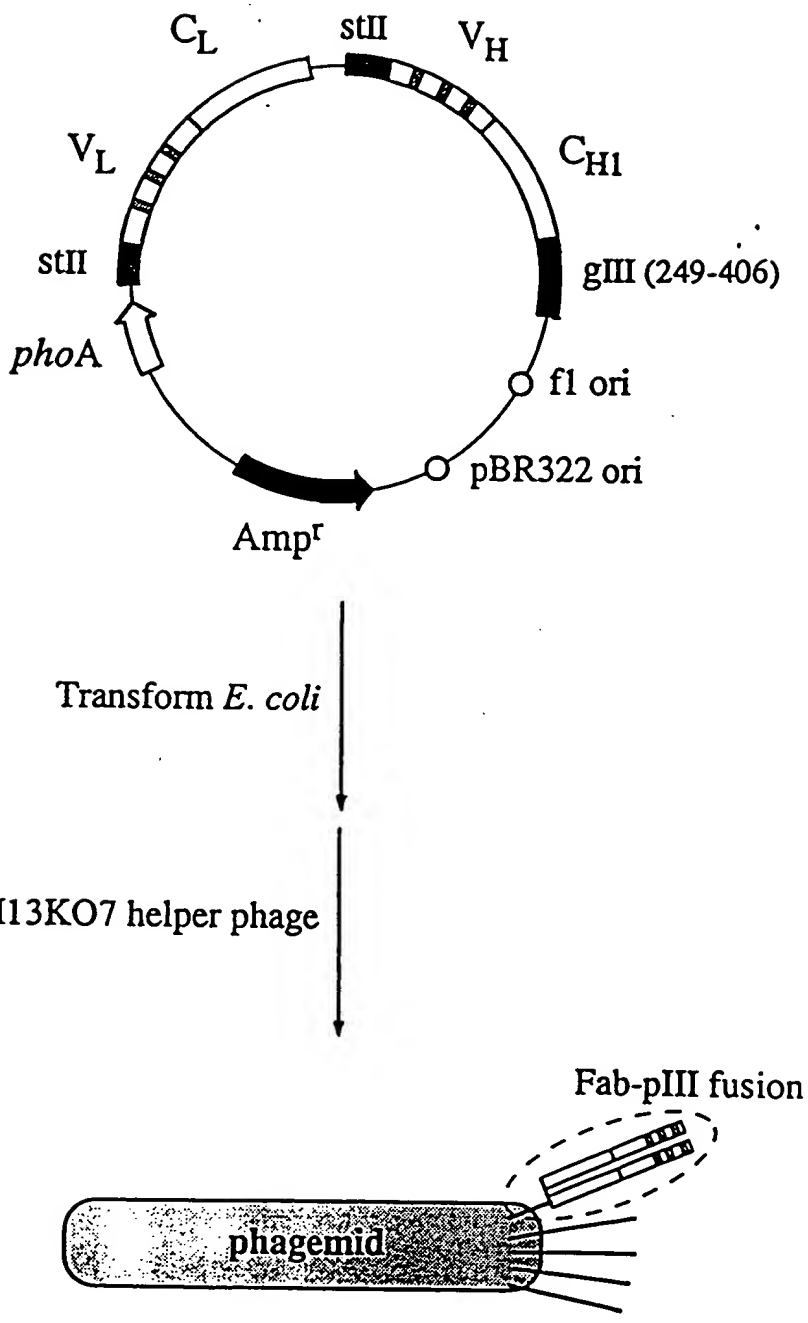
C_L
stII
V_H
V_L
C_{H1}
stII
gIII (249-406)
*pho*A
f1 ori
pBR322 ori
Amp^r
Transform *E. coli*
+ M13KO7 helper phage
Fab-pIII fusion
phagemid

Fig. 7

```
   1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTTGGA GATTATCGTC ACTGCAATGC
     CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAAACCT CTAATAGCAG TGACGTTACG

 101 TTCGCAATAT GGCGCAAAAT GACCAACAGC GGTTGATTGA TCAGGTAGAG GGGGCGCTGT ACGAGGTAAA GCCCGATGCC AGCATTCCTG ACGACGATAC
     AAGCGTTATA CCGCGTTTTA CTGGTTGTCG CCAACTAACT AGTCCATCTC CCCCGCGACA TGCTCCATTT CGGGCTACGG TCGTAAGGAC TGCTGCTATG

 201 GGAGCTGCTG CGCGATTACG TAAAGAAGTT ATTGAAGCAT CCTCGTCAGT AAAAAGTTAA TCTTTTCAAC AGCTGTCATA AAGTTGTCAC GGCCGAGACT
     CCTCGACGAC GCGCTAATGC ATTTCTTCAA TAACTTCGTA GGAGCAGTCA TTTTTCAATT AGAAAAGTTG TCGACAGTAT TTCAACAGTG CCGGCTCTGA

 301 TATAGTCGCT TTGTTTTTAT TTTTTAATGT ATTTGTAACT AGAATTCGAG CTCGGTACCC GGGGATCCTC TAGAGGTTGA GGTGATTTTA TGAAAAAGAA
     ATATCAGCGA AACAAAAATA AAAAATTACA TAAACATTGA TCTTAAGCTC GAGCCATGGG CCCCTAGGAG ATCTCCAACT CCACTAAAAT ACTTTTTCTT
-23                                                                                                    M etLysLysAsn
                                                                                                Begin stII signal sequence
 401 TATCGCATTT CTTCTTGCAT CTATGTTCGT TTTTTCTATT GCTACAAACG CGTACGCTGA TATCCAGTTG ACCCAGTCCC CGAGCTCCCT GTCCGCCTCT
     ATAGCGTAAA GAAGAACGTA GATACAAGCA AAAAAGATAA CGATGTTTGC GCATGCGACT ATAGGTCAAC TGGGTCAGGG GCTCGAGGGA CAGGCGGAGA
-19  IleAlaPhe LeuLeuAlaS erMetPheVa lPheSerIle AlaThrAsnA laTyrAlaAs pIleGlnLeu ThrGlnSerP roSerSerLe uSerAlaSer
                                                                Begin light chain
 501 GTGGGCGATA GGGTCACCAT CACCTGCAGC GCAAGTCAGG ATATTAGCAA CTATTTAAAC TGGTATCAAC AGAAACCAGG AAAAGCTCCG AAACTACTGA
     CACCCGCTAT CCCAGTGGTA GTGGACGTCG CGTTCAGTCC TATAATCGTT GATAAATTTG ACCATAGTTG TCTTTGGTCC TTTTCGAGGC TTTGATGACT
  15 ValGlyAspA rgValThrIl eThrCysSer AlaSerGlnA spIleSerAs nTyrLeuAsn TrpTyrGlnG lnLysProGl yLysAlaPro LysLeuLeuIle

 601 TTTACTTCAC CTCCTCTCTC CACTCTGGAG TCCCTTCTCG CTTCTCTGGA TCCGGTTCTG GGACGGATTA CACTCTGACC ATCAGCAGTC TGCAGCCAGA
     AAATGAAGTG GAGGAGAGAG GTGAGACCTC AGGGAAGAGC GAAGAGACCT AGGCCAAGAC CCTGCCTAAT GTGAGACTGG TAGTCGTCAG ACGTCGGTCT
  49   TyrPheTh rSerSerLeu HisSerGlyV alProSerAr gPheSerGly SerGlySerG lyThrAspTy rThrLeuThr IleSerSerL euGlnProGlu

 701 AGACTTCGCA ACTTATTACT GTCAACAGTA TAGCACCGTG CCGTGGACGT TTGGACAGGG TACCAAGGTG GAGATCAAAC GAACTGTGGC TGCACCATCT
     TCTGAAGCGT TGAATAATGA CAGTTGTCAT ATCGTGGCAC GGCACCTGCA AACCTGTCCC ATGGTTCCAC CTCTAGTTTG CTTGACACCG ACGTGGTAGA
  82  AspPheAla ThrTyrTyrC ysGlnGlnTy rSerThrVal ProTrpThrP heGlyGlnGl yThrLysVal GluIleLysA rgThrValAl aAlaProSer

 801 GTCTTCATCT TCCCGCCATC TGATGAGCAG TTGAAATCTG GAACTGCTTC TGTTGTGTGC CTGCTGAATA ACTTCTATCC CAGAGAGGCC AAAGTACAGT
     CAGAAGTAGA AGGGCGGTAG ACTACTCGTC AACTTTAGAC CTTGACGAAG ACAACACACG GACGACTTAT TGAAGATAGG GTCTCTCCGG TTTCATGTCA
 115 ValPheIleP heProProSe rAspGluGln LeuLysSerG lyThrAlaSe rValValCys LeuLeuAsnA snPheTyrPr oArgGluAla LysValGlnTrp

 901 GGAAGGTGGA TAACGCCCTC CAATCGGGTA ACTCCCAGGA GAGTGTCACA GAGCAGGACA GCAAGGACAG CACCTACAGC CTCAGCAGCA CCCTGACGCT
     CCTTCCACCT ATTGCGGGAG GTTAGCCCAT TGAGGGTCCT CTCACAGTGT CTCGTCCTGT CGTTCCTGTC GTGGATGTCG GAGTCGTCGT GGGACTGCGA
 149   LysValAs pAsnAlaLeu GlnSerGlyA snSerGlnGl uSerValThr GluGlnAspS erLysAspSe rThrTyrSer LeuSerSerT hrLeuThrLeu

1001 GAGCAAAGCA GACTACGAGA AACACAAAGT CTACGCCTGC GAAGTCACCC ATCAGGGCCT GAGCTCGCCC GTCACAAAGA GCTTCAACAG GGGAGAGTGT
     CTCGTTTCGT CTGATGCTCT TTGTGTTTCA GATGCGGACG CTTCAGTGGG TAGTCCCGGA CTCGAGCGGG CAGTGTTTCT CGAAGTTGTC CCCTCTCACA
 182  SerLysAla AspTyrGluL ysHisLysVa lTyrAlaCys GluValThrH isGlnGlyLe uSerSerPro ValThrLysS erPheAsnAr gGlyGluCys
```

Fig. 8A

```
1101 TAAGCTGATC CTCTACGCCG GACGCATCGT GGCCCTAGTA CGCAACTAGT CGTAAAAAGG GTATCTAGAG GTTGAGGTGA TTTTATGAAA AAGAATATCG
     ATTCGACTAG GAGATGCGGC CTGCGTAGCA CCGGGATCAT GCGTTGATCA GCATTTTTCC CATAGATCTC CAACTCCACT AAAATACTTT TTCTTATAGC
 215 OC*                                                                                                  -23 MetLys LysAsnIleAla
                  Begin stII signal sequence
1201 CATTTCTTCT TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACGCGTAC GCTGAGGTTC AGCTGGTGGA GTCTGGCGGT GGCCTGGTGC AGCCAGGGGG
     GTAAAGAAGA ACGTAGATAC AAGCAAAAAA GATAACGATG TTTGCGCATG CGACTCCAAG TCGACCACCT CAGACCGCCA CCGGACCACG TCGGTCCCCC
  -17   PheLeuLe uAlaSerMet PheValPheS erIleAlaTh rAsnAlaTyr AlaGluValG lnLeuValGl uSerGlyGly GlyLeuValG lnProGlyGly
                                                                  Begin heavy chain
1301 CTCACTCCGT TTGTCCTGTG CAGCTTCTGG CTATACCTTC ACCAACTATG GTATGAACTG GATCCGTCAG GCCCCGGGTA AGGGCCTGGA ATGGGTTGGA
     GAGTGAGGCA AACAGGACAC GTCGAAGACC GATATGGAAG TGGTTGATAC CATACTTGAC CTAGGCAGTC CGGGGCCCAT TCCCGGACCT TACCCAACCT
   17  SerLeuArg LeuSerCysA laAlaSerGl yTyrThrPhe ThrAsnTyrG lyMetAsnTr pIleArgGln AlaProGlyL ysGlyLeuGl uTrpValGly

1401 TGGATTAACA CCTATACCGG TGAACCGACC TATGCTGCGG ATTTCAAACG TCGTTTTACT ATATCTGCAG ACACCTCCAG CAACACAGTT TACCTGCAGA
     ACCTAATTGT GGATATGGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAAATGA TATAGACGTC TGTGGAGGTC GTTGTGTCAA ATGGACGTCT
   50 TrpIleAsnT hrTyrThrGl yGluProThr TyrAlaAlaA spPheLysAr gArgPheThr IleSerAlaA spThrSerSe rAsnThrVal TyrLeuGlnMet

1501 TGAACAGCCT GCGCGCTGAG GACACTGCCG TCTATTACTG TGCAAAGTAC CCGCACTATT ATGGGAGCAG CCACTGGTAT TTCGACGTCT GGGGTCAAGG
     ACTTGTCGGA CGCGCGACTC CTGTGACGGC AGATAATGAC ACGTTTCATG GGCGTGATAA TACCCTCGTC GGTGACCATA AAGCTGCAGA CCCCAGTTCC
   84   AsnSerLe uArgAlaGlu AspThrAlaV alTyrTyrCy sAlaLysTyr ProHisTyrT yrGlySerSe rHisTrpTyr PheAspValT rpGlyGlnGly

1601 AACCCTGGTC ACCGTCTCCT CGGCCTCCAC CAAGGGCCCA TCGGTCTTCC CCCTGGCACC CTCCTCCAAG AGCACCTCTG GGGGCACAGC GGCCCTGGGC
     TTGGGACCAG TGGCAGAGGA GCCGGAGGTG GTTCCCGGGT AGCCAGAAGG GGGACCGTGG GAGGAGGTTC TCGTGGAGAC CCCCGTGTCG CCGGGACCCG
  117  ThrLeuVal ThrValSerS erAlaSerTh rLysGlyPro SerValPheP roLeuAlaPr oSerSerLys SerThrSerG lyGlyThrAl aAlaLeuGly

1701 TGCCTGGTCA AGGACTACTT CCCCGAACCG GTGACGGTGT CGTGGAACTC AGGCGCCCTG ACCAGCGGCG TGCACACCTT CCCGGCTGTC CTACAGTCCT
     ACGGACCAGT TCCTGATGAA GGGGCTTGGC CACTGCCACA GCACCTTGAG TCCGCGGGAC TGGTCGCCGC ACGTGTGGAA GGGCCGACAG GATGTCAGGA
  150 CysLeuValL ysAspTyrPh eProGluPro ValThrValS erTrpAsnSe rGlyAlaLeu ThrSerGlyV alHisThrPh eProAlaVal LeuGlnSerSer

1801 CAGGACTCTA CTCCCTCAGC AGCGTGGTGA CCGTGCCCTC CAGCAGCTTG GGCACCCAGA CCTACATCTG CAACGTGAAT CACAAGCCCA GCAACACCAA
     GTCCTGAGAT GAGGGAGTCG TCGCACCACT GGCACGGGAG GTCGTCGAAC CCGTGGGTCT GGATGTAGAC GTTGCACTTA GTGTTCGGGT CGTTGTGGTT
  184   GlyLeuTy rSerLeuSer SerValValT hrValProSe rSerSerLeu GlyThrGlnT hrTyrIleCy sAsnValAsn HisLysProS erAsnThrLys

1901 GGTCGACAAG AAAGTTGAGC CCAAATCTTG TGACAAAACT CACCTCTAGA GTGGCGGTGG CTCTGGTTCC GGTGATTTTG ATTATGAAAA GATGGCAAAC
     CCAGCTGTTC TTTCAACTCG GGTTTAGAAC ACTGTTTTGA GTGGAGATCT CACCGCCACC GAGACCAAGG CCACTAAAAC TAATACTTTT CTACCGTTTG
  217  ValAspLys LysValGluP roLysSerCy sAspLysThr HisLeuAM*S erGlyGlyGl ySerGlySer GlyAspPheA spTyrGluLy sMetAlaAsn
                                        end light chain   Begin g3p domain
2001 GCTAATAAGG GGGCTATGAC CGAAAATGCC GATGAAAACG CGCTACAGTC TGACGCTAAA GGCAAACTTG ATTCTGTCGC TACTGATTAC GGTGCTGCTA
     CGATTATTCC CCCGATACTG GCTTTTACGG CTACTTTTGC GCGATGTCAG ACTGCGATTT CCGTTTGAAC TAAGACAGCG ATGACTAATG CCACGACGAT
  250 AlaAsnLysG lyAlaMetTh rGluAsnAla AspGluAsnA laLeuGlnSe rAspAlaLys GlyLysLeuA spSerValAl aThrAspTyr GlyAlaAlaIle

2101 TCGATGGTTT CATTGGTGAC GTTTCCGGCC TTGCTAATGG TAATGGTGCT ACTGGTGATT TTGCTGGCTC TAATTCCCAA ATGGCTCAAG TCGGTGACGG
     AGCTACCAAA GTAACCACTG CAAAGGCCGG AACGATTACC ATTACCACGA TGACCACTAA AACGACCGAG ATTAAGGGTT TACCGAGTTC AGCCACTGCC
  284   AspGlyPh eIleGlyAsp ValSerGlyL euAlaAsnGl yAsnGlyAla ThrGlyAspP heAlaGlySe rAsnSerGln MetAlaGlnV alGlyAspGly

2201 TGATAATTCA CCTTTAATGA ATAATTTCCG TCAATATTTA CCTTCCCTCC CTCAATCGGT TGAATGTCGC CCTTTTGTCT TTAGCGCTGG TAAACCATAT
     ACTATTAAGT GGAAATTACT TATTAAAGGC AGTTATAAAT GGAAGGGAGG GAGTTAGCCA ACTTACAGCG GGAAAACAGA AATCGCGACC ATTTGGTATA
  317  AspAsnSer ProLeuMetA snAsnPheAr gGlnTyrLeu ProSerLeuP roGlnServa lGluCysArg ProPheValP heSerAlaGl yLysProTyr
```

Fig. 8B

```
2301 GAATTTTCTA TTGATTGTGA CAAAATAAAC TTATTGCGTG GTGTCTTTGC GTTTGTTTTA TATGTTGCCA CCTTTATGTA TGTATTTTCT ACGTTTGCTA
     CTTAAAAGAT AACTAACACT GTTTTATTTG AATAAGGCAC CACAGAAACG CAAAGAAAAT ATACAACGGT GGAAATACAT ACATAAAAGA TGCAAACGAT
 350 GluPheSerI leAspCysAs pLysIleAsn LeuPheArgG lyValPheAl aPheLeuLeu TyrValAlaT hrPheMetTy rValPheSer ThrPheAlaAsn

2401 ACATACTGCG TAATAAGGAG TCTTAATCAT GCCAGTTCTT TTGGCTAGCG CCGCCCTATA CCTTGTCTGC CTCCCCGCGT TGCGTCGCGG TGCATGGAGC
     TGTATGACGC ATTATTCCTC AGAATTAGTA CGGTCAAGAA AACCGATCGC GGCGGGATAT GGAACAGACG GAGGGGCGCA ACGCAGCGCC ACGTACCTCG
 384   IleLeuAr gAsnLysGlu SerOC* (SEQ ID NO: 100)
                 end g3 protein
2501 CGGGCCACCT CGACCTGAAT GGAAGCCGGC GGCACCTCGC TAACGGATTC ACCACTCCAA GAATTGGAGC CAATCAATTC TTGCGGAGAA CTGTGAATGC
     GCCCGGTGGA GCTGGACTTA CCTTCGGCCG CCGTGGAGCG ATTGCCTAAG TGGTGAGGTT CTTAACCTCG GTTAGTTAAG AACGCCTCTT GACACTTACG

2601 GCAAACCAAC CCTTGGCAGA ACATATCCAT CGCGTCCGCC ATCTCCAGCA GCCGCACGCG GCGCATCTCG GGCAGCGTTG GGTCCTGGCC ACGGGTGCGC
     CGTTTGGTTG GGAACCGTCT TGTATAGGTA GCGCAGGCGG TAGAGGTCGT CGGCGTGCGC CGCGTAGAGC CCGTCGCAAC CCAGGACCGG TGCCCACGCG

2701 ATGATCGTGC TCCTGTCGTT GAGGACCCGG CTAGGCTGGC GGGGTTGCCT TACTGGTTAG CAGAATGAAT CACCGATACG CGAGCGAACG TGAAGCGACT
     TACTAGCACG AGGACAGCAA CTCCTGGGCC GATCCGACCG CCCCAACGGA ATGACCAATC GTCTTACTTA GTGGCTATGC GCTCGCTTGC ACTTCGCTGA

2801 GCTGCTGCAA AACGTCTGCG ACCTGAGCAA CAACATGAAT GGTCTTCGGT TTCCGTGTTT CGTAAAGTCT GGAAACGCGG AAGTCAGCGC CCTGCACCAT
     CGACGACGTT TTGCAGACGC TGGACTCGTT GTTGTACTTA CCAGAAGCCA AAGGCACAAA GCATTTCAGA CCTTTGCGCC TTCAGTCGCG GGACGTGGTA

2901 TATGTTCCGG ATCTGCATCG CAGGATGCTG CTGGCTACCC TGTGGAACAC CTACATCTGT ATTAACGAAG CGCTGGCATT GACCCTGAGT GATTTTTCTC
     ATACAAGGCC TAGACGTAGC GTCCTACGAC GACCGATGGG ACACCTTGTG GATGTAGACA TAATTGCTTC GCGACCGTAA CTGGGACTCA CTAAAAAGAG

3001 TGGTCCCGCC GCATCCATAC CGCCAGTTGT TTACCCTCAC AACGTTCCAG TAACCGGGCA TGTTCATCAT CAGTAACCCG TATCGTGAGC ATCCTCTCTC
     ACCAGGGCGG CGTAGGTATG GCGGTCAACA AATGGGAGTG TTGCAAGGTC ATTGGCCCGT ACAAGTAGTA GTCATTGGGC ATAGCACTCG TAGGAGAGAG

3101 GTTTCATCGG TATCATTACC CCCATGAACA GAAATTCCCC CTTACACGGA GGCATCAAGT GACCAAACAG GAAAAAACCG CCCTTAACAT GGCCCGCTTT
     CAAAGTAGCC ATAGTAATGG GGGTACTTGT CTTTAAGGGG GAATGTGCCT CCGTAGTTCA CTGGTTTGTC CTTTTTTGGC GGGAATTGTA CCGGGCGAAA

3201 ATCAGAAGCC AGACATTAAC GCTTCTGGAG AAACTCAACG AGCTGGACGC GGATGAACAG GCAGACATCT GTGAATCGCT TCACGACCAC GCTGATGAGC
     TAGTCTTCGG TCTGTAATTG CGAAGACCTC TTTGAGTTGC TCGACCTGCG CCTACTTGTC CGTCTGTAGA CACTTAGCGA AGTGCTGGTG CGACTACTCG

3301 TTTACCGCAG GATCCGGAAA TTGTAAACGT TAATATTTTG TTAAAATTCG CGTTAAATTT TTGTTAAATC AGCTCATTTT TTAACCAATA GGCCGAAATC
     AAATGGCGTC CTAGGCCTTT AACATTTGCA ATTATAAAAC AATTTTAAGC GCAATTTAAA AACAATTTAG TCGAGTAAAA AATTGGTTAT CCGGCTTTAG

3401 GGCAAAATCC CTTATAAATC AAAAGAATAG ACCGAGATAG GGTTGAGTGT TGTTCCAGTT TGGAACAAGA GTCCACTATT AAAGAACGTG GACTCCAACG
     CCGTTTTAGG GAATATTTAG TTTTCTTATC TGGCTCTATC CCAACTCACA ACAAGGTCAA ACCTTGTTCT CAGGTGATAA TTTCTTGCAC CTGAGGTTGC

3501 TCAAAGGGCG AAAAACCGTC TATCAGGGCT ATGGCCCACT ACGTGAACCA TCACCCTAAT CAAGTTTTTT GGGGTCGAGG TGCCGTAAAG CACTAAATCG
     AGTTTCCCGC TTTTTGGCAG ATAGTCCCGA TACCGGGTGA TGCACTTGGT AGTGGGATTA GTTCAAAAAA CCCCAGCTCC ACGGCATTTC GTGATTTAGC

3601 GAACCCTAAA GGGAGCCCCC GATTTAGAGC TTGACGGGGA AAGCCGGCGA ACGTGGCGAG AAAGGAAGGG AAGAAAGCGA AAGGAGCGGG CGCTAGGGCG
     CTTGGGATTT CCCTCGGGGG CTAAATCTCG AACTGCCCCT TTCGGCCGCT TGCACCGCTC TTTCCTTCCC TTCTTTCGCT TTCCTCGCCC GCGATCCCGC

3701 CTGGCAAGTG TAGCGGTCAC GCTGCGCGTA ACCACCACAC CCGCCGCGCT TAATGCGCCG CTACAGGGCG CGTCCGGATC CTGCCTCGCG CGTTTCGGTG
     GACCGTTCAC ATCGCCAGTG CGACGCGCAT TGGTGGTGTG GGCGGCGCGA ATTACGCGGC GATGTCCCGC GCAGGCCTAG GACGGAGCGC GCAAAGCCAC

3801 ATGACGGTGA AAACCTCTGA CACATGCAGC TCCCGGAGAC GGTCACAGCT TGTCTGTAAG CGGATGCCGG GAGCAGACAA GCCCGTCAGG GCGCGTCAGC
     TACTGCCACT TTTGGAGACT GTGTACGTCG AGGGCCTCTG CCAGTGTCGA ACAGACATTC GCCTACGGCC CTCGTCTGTT CGGGCAGTCC CGCGCAGTCG
```

Fig. 8C

```
3901 GGGTGTTGGC GGGTGTCGGG GCGCAGCCAT GACCCAGTCA CGTAGCGATA GCGGAGTGTA TACTGGCTTA ACTATGCGGC ATCAGAGCAG ATTGTACTGA
     CCCACAACCG CCCACAGCCC CGCGTCGGTA CTGGGTCAGT GCATCGCTAT CGCCTCACAT ATGACCGAAT TGATACGCCG TAGTCTCGTC TAACATGACT

4001 GAGTGCACCA TATGCGGTGT GAAATACCGC ACAGATGCGT AAGGAGAAAA TACCGCATCA GGCGCTCTTC CGCTTCCTCG CTCACTGACT CGCTGCGCTC
     CTCACGTGGT ATACGCCACA CTTTATGGCG TGTCTACGCA TTCCTCTTTT ATGGCGTAGT CCGCGAGAAG GCGAAGGAGC GAGTGACTGA GCGACGCGAG

4101 GGTCGTTCGG CTGCGGCGAG CGGTATCAGC TCACTCAAAG GCGGTAATAC GGTTATCCAC AGAATCAGGG GATAACGCAG GAAAGAACAT GTGAGCAAAA
     CCAGCAAGCC GACGCCGCTC GCCATAGTCG AGTGAGTTTC CGCCATTATG CCAATAGGTG TCTTAGTCCC CTATTGCGTC CTTTCTTGTA CACTCGTTTT

4201 GGCCAGCAAA AGGCCAGGAA CCGTAAAAAG GCCGCGTTGC TGGCGTTTTT CCATAGGCTC CGCCCCCCTG ACGAGCATCA CAAAAATCGA CGCTCAAGTC
     CCGGTCGTTT TCCGGTCCTT GGCATTTTTC CGGCGCAACG ACCGCAAAAA GGTATCCGAG GCGGGGGGAC TGCTCGTAGT GTTTTTAGCT GCGAGTTCAG

4301 AGAGGTGGCG AAACCCGACA GGACTATAAA GATACCAGGC GTTTCCCCCT GGAAGCTCCC TCGTGCGCTC TCCTGTTCCG ACCCTGCCGC TTACCGGATA
     TCTCCACCGC TTTGGGCTGT CCTGATATTT CTATGGTCCG CAAAGGGGGA CCTTCGAGGG AGCACGCGAG AGGACAAGGC TGGGACGGCG AATGGCCTAT

4401 CCTGTCCGCC TTTCTCCCTT CGGGAAGCGT GGCGCTTTCT CATAGCTCAC GCTGTAGGTA TCTCAGTTCG GTGTAGGTCG TTCGCTCCAA GCTGGGCTGT
     GGACAGGCGG AAAGAGGGAA GCCCTTCGCA CCGCGAAAGA GTATCGAGTG CGACATCCAT AGAGTCAAGC CACATCCAGC AAGCGAGGTT CGACCCGACA

4501 GTGCACGAAC CCCCCGTTCA GCCCGACCGC TGCGCCTTAT CCGGTAACTA TCGTCTTGAG TCCAACCCGG TAAGACACGA CTTATCGCCA CTGGCAGCAG
     CACGTGCTTG GGGGGCAAGT CGGGCTGGCG ACGCGGAATA GGCCATTGAT AGCAGAACTC AGGTTGGGCC ATTCTGTGCT GAATAGCGGT GACCGTCGTC

4601 CCACTGGTAA CAGGATTAGC AGAGCGAGGT ATGTAGGCGG TGCTACAGAG TTCTTGAAGT GGTGGCCTAA CTACGGCTAC ACTAGAAGGA CAGTATTTGG
     GGTGACCATT GTCCTAATCG TCTCGCTCCA TACATCCGCC ACGATGTCTC AAGAACTTCA CCACCGGATT GATGCCGATG TGATCTTCCT GTCATAAACC

4701 TATCTGCGCT CTGCTGAAGC CAGTTACCTT CGGAAAAAGA GTTGGTAGCT CTTGATCCGG CAAACAAACC ACCGCTGGTA GCGGTGGTTT TTTTGTTTGC
     ATAGACGCGA GACGACTTCG GTCAATGGAA GCCTTTTTCT CAACCATCGA GAACTAGGCC GTTTGTTTGG TGGCGACCAT CGCCACCAAA AAAACAAACG

4801 AAGCAGCAGA TTACGCGCAG AAAAAAAGGA TCTCAAGAAG ATCCTTTGAT CTTTTCTACG GGGTCTGACG CTCAGTGGAA CGAAAACTCA CGTTAAGGGA
     TTCGTCGTCT AATGCGCGTC TTTTTTTCCT AGAGTTCTTC TAGGAAACTA GAAAAGATGC CCCAGACTGC GAGTCACCTT GCTTTTGAGT GCAATTCCCT

4901 TTTTGGTCAT GAGATTATCA AAAAGGATCT TCACCTAGAT CCTTTTAAAT TAAAAATGAA GTTTTAAATC AATCTAAAGT ATATATGAGT AAACTTGGTC
     AAAACCAGTA CTCTAATAGT TTTTCCTAGA AGTGGATCTA GGAAAATTTA ATTTTTACTT CAAAATTTAG TTAGATTTCA TATATACTCA TTTGAACCAG

5001 TGACAGTTAC CAATGCTTAA TCAGTGAGGC ACCTATCTCA GCGATCTGTC TATTTCGTTC ATCCATAGTT GCCTGACTCC CCGTCGTGTA GATAACTACG
     ACTGTCAATG GTTACGAATT AGTCACTCCG TGGATAGAGT CGCTAGACAG ATAAAGCAAG TAGGTATCAA CGGACTGAGG GGCAGCACAT CTATTGATGC

5101 ATACGGGAGG GCTTACCATC TGGCCCCAGT GCTGCAATGA TACCGCGAGA CCCACGCTCA CCGGCTCCAG ATTTATCAGC AATAAACCAG CCAGCCGGAA
     TATGCCCTCC CGAATGGTAG ACCGGGGTCA CGACGTTACT ATGGCGCTCT GGGTGCGAGT GGCCGAGGTC TAAATAGTCG TTATTTGGTC GGTCGGCCTT

5201 GGGCCGAGCG CAGAAGTGGT CCTGCAACTT TATCCGCCTC CATCCAGTCT ATTAATTGTT GCCGGGAAGC TAGAGTAAGT AGTTCGCCAG TTAATAGTTT
     CCCGGCTCGC GTCTTCACCA GGACGTTGAA ATAGGCGGAG GTAGGTCAGA TAATTAACAA CGGCCCTTCG ATCTCATTCA TCAAGCGGTC AATTATCAAA

5301 GCGCAACGTT GTTGCCATTG CTGCAGGCAT CGTGGTGTCA CGCTCGTCGT TTGGTATGGC TTCATTCAGC TCCGGTTCCC AACGATCAAG GCGAGTTACA
     CGCGTTGCAA CAACGGTAAC GACGTCCGTA GCACCACAGT GCGAGCAGCA AACCATACCG AAGTAAGTCG AGGCCAAGGG TTGCTAGTTC CGCTCAATGT

5401 TGATCCCCCA TGTTGTGCAA AAAAGCGGTT AGCTCCTTCG GTCCTCCGAT CGTTGTCAGA AGTAAGTTGG CCGCAGTGTT ATCACTCATG GTTATGGCAG
     ACTAGGGGGT ACAACACGTT TTTTCGCCAA TCGAGGAAGC CAGGAGGCTA GCAACAGTCT TCATTCAACC GGCGTCACAA TAGTGAGTAC CAATACCGTC

5501 CACTGCATAA TTCTCTTACT GTCATGCCAT CCGTAAGATG CTTTTCTGTG ACTGGTGAGT ACTCAACCAA GTCATTCTGA GAATAGTGTA TGCGGCGACC
     GTGACGTATT AAGAGAATGA CAGTACGGTA GGCATTCTAC GAAAAGACAC TGACCACTCA TGAGTTGGTT CAGTAAGACT CTTATCACAT ACGCCGCTGG
```

Fig. 8D

```
5601 GAGTTGCTCT TGCCCGGCGT CAACACGGGA TAATACCGCG CCACATAGCA GAACTTTAAA AGTGCTCATC ATTGGAAAAC GTTCTTCGGG GCGAAAACTC
     CTCAACGAGA ACGGGCCGCA GTTGTGCCCT ATTATGGCGC GGTGTATCGT CTTGAAATTT TCACGAGTAG TAACCTTTTG CAAGAAGCCC CGCTTTTGAG

5701 TCAAGGATCT TACCGCTGTT GAGATCCAGT TCGATGTAAC CCACTCGTGC ACCCAACTGA TCTTCAGCAT CTTTTACTTT CACCAGCGTT TCTGGGTGAG
     AGTTCCTAGA ATGGCGACAA CTCTAGGTCA AGCTACATTG GGTGAGCACG TGGGTTGACT AGAAGTCGTA GAAAATGAAA GTGGTCGCAA AGACCCACTC

5801 CAAAAACAGG AAGGCAAAAT GCCGCAAAAA AGGGAATAAG GGCGACACGG AAATGTTGAA TACTCATACT CTTCCTTTTT CAATATTATT GAAGCATTTA
     GTTTTTGTCC TTCCGTTTTA CGGCGTTTTT TCCCTTATTC CCGCTGTGCC TTTACAACTT ATGAGTATGA GAAGGAAAAA GTTATAATAA CTTCGTAAAT

5901 TCAGGGTTAT TGTCTCATGA GCGGATACAT ATTTGAATGT ATTTAGAAAA ATAAACAAAT AGGGGTTCCG CGCACATTTC CCCGAAAAGT GCCACCTGAC
     AGTCCCAATA ACAGAGTACT CGCCTATGTA TAAACTTACA TAAATCTTTT TATTTGTTTA TCCCCAAGGC GCGTGTAAAG GGGCTTTTCA CGGTGGACTG

6001 GTCTAAGAAA CCATTATTAT CATGACATTA ACCTATAAAA ATAGGCGTAT CACGAGGCCC TTTCGTCTTC AA (SEQ ID NO: 99)
     CAGATTCTTT GGTAATAATA GTACTGTAAT TGGATATTTT TATCCGCATA GTGCTCCGGG AAAGCAGAAG TT
```

Fig. 8E

▨ = differences from F(ab)-12

```
                        10                  20                  30
F(ab)-12 DIQMTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQ
MB1.6    DIQLTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQ
H2305.6  DIQLTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQ
Y0101    DIQLTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQ
Y0192    DIQLTQSPSSLSASVGDRVTITCRANEQISNYLNWYQQ
                                    CDR-L1
                    40          50          60          70
F(ab)-12 KPGKAPKVLIYFTSSLHSGVPSRFSGSGSGTDFTLTIS
MB1.6    KPGKAPKLLIYFTSSLHSGVPSRFSGSGSGTDVTLTIS
H2305.6  KPGKAPKVLIYFTSSLHSGVPSRFSGSGSGTDVTLTIS
Y0101    KPGKAPKVLIYFTSSLHSGVPSRFSGSGSGTDFTLTIS
Y0192    KPGKAPKVLIYFTSSLHSGVPSRFSGSGSGTDFTLTIS
                CDR-L2
                80          90          100
F(ab)-12 SLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTV (SEQ ID NO:8)
MB1.6    SLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTV (SEQ ID NO: 101)
H2305.6  SLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTV (SEQ ID NO:103)
Y0101    SLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTV (SEQ ID NO:105)
Y0192    SLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTV (SEQ ID NO: 107)
                        CDR-L3
```

Fig. 9A

```
                        10                  20                  30
F(ab)-12 EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWVR
MB1.6    EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWIR
H2305.6  EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWIR
Y0101    EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWVR
Y0192    EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGINWVR
                                    CDR-H1
                    40          50          60          70
F(ab)-12 QAPGKGLEWVGWINTYTGEPTYAADFKRRFTFSLDTSKSTA
MB1.6    QAPGKGLEWVGWINTYTGEPTYAADFKRRFTISADTSSNIV
H2305.6  QAPGKGLEWVGWINTYTGEPTYAADFKRRFTFSADTSSNIV
Y0101    QAPGKGLEWVGWINTYTGEPTYAADFKRRFTFSLDTSKSTA
Y0192    QAPGKGLEWVGWINTYTGEPTYAADFKRRFTFSLDTSKSTA
                        CDR-H2                  CDR-7
                80          90          100         110
F(ab)-12 YLQMNSLRAEDTAVYYCAKYPHYYGSSHWYFDVWGQGTL (SEQ ID NO:7)
MB1.6    YLQMNSLRAEDTAVYYCAKYPHYYGSSHWYFDVWGQGTL (SEQ ID NO: 102)
H2305.6  YLQMNSLRAEDTAVYYCAKYPHYYGSSHWYFDVWGQGTL (SEQ ID NO: 104)
Y0101    YLQMNSLRAEDTAVYYCAKYPHYYGSSHWYFDVWGQGTL (SEQ ID NO: 106)
Y0192    YLQMNSLRAEDTAVYYCAKYPHYYGSSHWYFDVWGQGTL (SEQ ID NO: 108)
                                    CDR-H3
```

Fig. 9B

▨ = differences from)-12

```
                          10                  20                  30
F(ab)-12 DIQMTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQ
Y0243-1  DIQLTQSPSSLSASVGDRVTITCRANEQLSNYLNWYQQ
Y0238-3  DIQLTQSPSSLSASVGDRVTITCRANEQLSNYLNWYQQ
Y0313-1  DIQLTQSPSSLSASVGDRVTITCRANEQLSNYLNWYQQ
Y0317    DIQLTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQ
                                        CDR-L1
                 40                  50                  60                  70
F(ab)-12 KPGKAPKVLIYFTSSLHSGVPSRFSGSGSGTDFTLTIS
Y0243-1  KPGKAPKVLIYFTSSLHSGVPSRFSGSGSGTDFTLTIS
Y0238-3  KPGKAPKVLIYFTSSLHSGVPSRFSGSGSGTDFTLTIS
Y0313-1  KPGKAPKVLIYFTSSLHSGVPSRFSGSGSGTDFTLTIS
Y0317    KPGKAPKVLIYFTSSLHSGVPSRFSGSGSGTDFTLTIS
                   CDR-L2
                 80                  90                  100
F(ab)-12 SLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTV (SEQ ID NO:8)
Y0243-1  SLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTV (SEQ ID NO:109)
Y0238-3  SLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTV (SEQ ID NO:111)
Y0313-1  SLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTV (SEQ ID NO:113)
Y0317    SLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTV (SEQ ID NO:115)
                        CDR-L3
```

Fig. 10A

```
                          10                  20                  30
F(ab)-12 EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWVR
Y0243-1  EVQLVESGGGLVQPGGSLRLSCAASGYDFTHYGMNWVR
Y0238-3  EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGINWVR
Y0313-1  EVQLVESGGGLVQPGGSLRLSCAASGYDFTHYGMNWVR
Y0317    EVQLVESGGGLVQPGGSLRLSCAASGYDFTHYGMNWVR
                                        CDR-H1
                 40                  50                  60                  70
F(ab)-12 QAPGKGLEWVGWINTYTGEPTYAADFKRRFTFSLDTSKSTA
Y0243-1  QAPGKGLEWVGWINTYTGEPTYAADFKRRFTFSLDTSKSTA
Y0238-3  QAPGKGLEWVGWINTYTGEPTYAADFKRRFTFSLDTSKSTA
Y0313-1  QAPGKGLEWVGWINTYTGEPTYAADFKRRFTFSLDTSKSTA
Y0317    QAPGKGLEWVGWINTYTGEPTYAADFKRRFTFSLDTSKSTA
                   CDR-H2                          CDR-7
                 80                  90                  100                 110
F(ab)-12 YLQMNSLRAEDTAVYYCAKYPHYYGSSHWYFDVWGQGTL (SEQ ID NO:7)
Y0243-1  YLQMNSLRAEDTAVYYCAKYPHYYGSSHWYFDVWGQGTL (SEQ ID NO:110)
Y0238-3  YLQMNSLRAEDTAVYYCAKYPYYYGTSHWYFDVWGQGTL (SEQ ID NO:112)
Y0313-1  YLQMNSLRAEDTAVYYCAKYPYYYGTSHWYFDVWGQGTL (SEQ ID NO:114)
Y0317    YLQMNSLRAEDTAVYYCAKYPYYYGTSHWYFDVWGQGTL (SEQ ID NO:116)
                                        CDR-H3
```

Fig. 10B

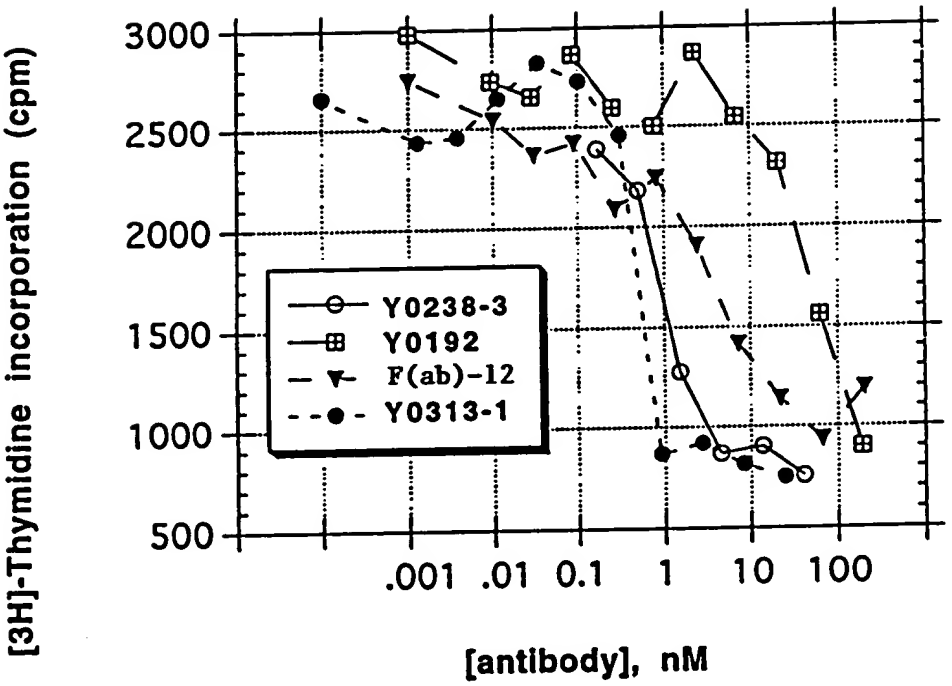
[3H]-Thymidine incorporation (cpm)
3000
2500
2000
1500
1000
500
.001
.01
0.1
1
10
100
[antibody], nM
Y0238-3
Y0192
F(ab)-12
Y0313-1

Fig. 11

Fig. 12